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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,283	08/16/2001	Usha Kasid	P 0280652 KAUS430501	9971

909 7590 10/23/2002

PILLSBURY WINTHROP, LLP
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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	8

DATE MAILED: 10/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/930,283	Applicant(s) KASID ET AL.	
	Examiner Terra C. Gibbs	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-25 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Preliminary Amendment A, filed 8/16/01 in Paper No. 5 has been acknowledged. Preliminary Amendment A requested the cancellation of claims 18-20, 23, 25, 27-33 and the addition of claims 34-41. However, claims 18-20, 23, 25, 27-33 were not present in the application at the time the 8/16/01 Amendment was filed.

Claims 34-41, filed 8/16/01, have been renumbered claims 18-25 in accordance with 37 CFR 1.126.

Claims 1-25 are pending in the instant application.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because:

> Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Nucleotide and/or Amino Acid Sequence Disclosure

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR §1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 §1.821 through 1.825 for the reason(s) set forth below. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 Fed. Reg. 18230, May 1, 1990. It is noted that the application fails to comply with 37 CFR §1.821(a) and (d).

Claims 4, 9, 15 and 16 contain sequences that are not identified by a SEQ ID NO. (see Claim Objections below). Additionally, page 3 contains a sequence that is not identified by a SEQ ID NO. The above are examples and are not intended to indicate that the examiner has made an exhaustive review of the application.

Applicant must comply with the sequence rules in response to the instant official action. Applicant must fully comply with the sequence rules for any response to this action to be considered fully responsive.

Claim Objections

Claim 4 is objected to because of the following informalities: The sequence: 5'-GTGCTCCCATTGATGC-3' is not identified in the sequence listing. It appears that applicants are intending to recite sequence: 5'-GTGCTCCATTGATGC-3'. Appropriate correction is required.

Claims 4, 9, 15 and 16 are objected to because of the following informalities: The sequences: 5'-GTGCTCCCATTGATGC-3' and 5'-GTGCTCCCATTGATGC-3' (assumed typographical sequence) should be identified by a SEQ ID NO. Appropriate correction is required.

Double Patenting

Claim 11 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 10. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim

to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 and 17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5, 6, 8 and 13 of U.S. Patent No. 6,126,965. Although the conflicting claims are not identical, they are not patentably distinct from each other because the composition comprising a cationic liposome containing a cationic lipid, phosphatidylcholine and cholesterol (claim 1), further comprising dimethyldioctadecyl ammonium bromide (DDAB) (claim 17), wherein the liposome contains a raf antisense (claims 2 and 3), wherein only the terminal sequences are phosphorothioated (claim 4), in a pharmaceutically acceptable carrier (claims 5-8), of the instant invention overlaps with the composition comprising cationic liposomes which consist essentially of phosphatidylcholine and cholesterol, further comprising dimethyldioctadecyl ammonium bromide (DDAB) and further having encapsulated at least one modified oligonucleotide (claims 1 and 13), wherein said

oligonucleotide is about 15 to 40 nucleotides long and is a raf antisense (claims 2, 5 and 6), further comprising a pharmaceutically acceptable carrier (claim 8) of '965.

Claims 9-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,333,314. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of radiosensitizing tumor tissue by administering an antisense oligonucleotide of no more than 40 bases containing the sequence 5'-GTGCTCCATTGATGC-3' (claim 9), wherein the oligonucleotide is phosphorothioated (claims 10, 11 and 15) and administered intravenously to the arterial supply of target tissue (claims 12-14) of the instant application overlaps with the method of radiosensitizing tumor tissue by administering a composition comprising a cationic liposome, phosphatidylcholine and cholesterol, and further comprising a radiosensitizing encapsulated antisense oligonucleotide of no more than 40 bases containing the sequence 5'-GTGCTCCATTGATGC-3' (claim 1), wherein the oligonucleotide is phosphorothioated (claims 2, 6 and 7) and administered intravenously to the arterial supply of the target tissue (claims 3-5) of '314.

Claim 16 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of U.S. Patent No. 6,333,314. Although the conflicting claims are not identical, they are not patentably distinct from each other because the composition of matter comprising liposomes containing the sequence

5'-GTGCTCCATTGATGC-3' in a pharmaceutically acceptable carrier of claim 16 of the instant invention overlaps with the composition of matter comprising lipsomes consisting essentially of DDAB, phosphatidylcholine, and cholesterol and containing the sequence 5'-GTGCTCCATTGATGC-3', wherein only the terminal sequences are phosphorothioated of claim 7 of '314.

Claims 18-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,333,314. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treating a patient having cancerous tumor tissue comprising radiosensitizing tumor tissue by administering a radiosensitizing composition comprising a cationic liposome, phosphatidylcholine and cholesterol further comprising an antisense oligonucleotide of no more than 40 bases that binds to an oncogene nucleic acid (claim 18), wherein the oligonucleotide is a ras, raf, cot, mos or myc oncogene (claims 19 and 20) of the instant application overlap with the method of radiosensitizing tumor tissue by administering a composition comprising a cationic liposome, phosphatidylcholine and cholesterol, and further comprising a radiosensitizing encapsulated antisense oligonucleotide of no more than 40 bases containing the sequence 5'-GTGCTCCATTGATGC-3' (the sequence being a specific raf oncogene sequence) of claim 1 of '314.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of administering antisense raf of the nucleotide sequence 5'-GTGCTCCATTGATGC-3' intratumorally in immunocompromised mice, does not reasonably provide enablement for the radiosensitization of all tumors in all organisms wherein an oligonucleotide is administered *in vivo* to all organisms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claimed invention is drawn to an (improved) method of treating cancer comprising the administration of therapeutic radiation and further comprising the administration of antisense oligonucleotides, specific to an oncogene, encapsulated in liposomes, to a whole organism *in vivo*.

The following factors have been considered in determining that the specification does not enable the skilled artisan to make and/or use the invention over the scope claimed. This determination is based on several factors which, when considered together, illustrates that the art of gene delivery, expression and/or inhibition is is highly unpredictable. The discussion is also based on references whose teachings show that, despite a tremendous amount of experimentation by highly skilled artisans in the field of gene delivery and expression *in vivo*, there remain significant hurdles known in the art to make and/or use the invention over the scope claimed.

(1) the nature of the invention;
(2) the state of the prior art and the predictability or unpredictability of the art;
(3) the amount of direction or guidance and the presence or absence of working examples;

(4) the breadth of the claims; and
(5) the quantity of experimentation required

(1) The nature of the invention. Methods of targeting nucleic acids into host cells *in vivo* fall into the broad area known as gene therapy methods. While delivery of nucleic acids in and of itself is not considered as therapy *per se, in vivo* delivery shares many of the obstacles recognized for the actual therapy methods because successful therapy methods are, for the most part, based on the ability to deliver exogenous nucleic acids to cells or tissues of interest.

(2) The state of the prior art and the predictability or unpredictability of the art. The following references are cited herein to illustrate the state of the art of gene delivery. Crystal (Science, 1995 Vol. 270:404-410) points out that some advantages of using plasmid-liposome complexes as gene transfer vectors include their general inefficiency at achieving successful gene transfer and a general lack of available data regarding repetitive administration of liposomes of DNA to whole organisms (see page 405, second paragraph). Schofield et al. (British Medical Bulletin, 1995 Vol. 51:56-71) also teach advantages of liposome delivery of genes *in vivo*, although many of the details regarding cell targeting, cell entry and gene expression in target cells remain highly speculative. Schofield et al. caution that there are significant variations that exist between animals *[emphasis added]*, and state that only limited conclusions could be drawn from animal studies which may be applied to the treatment of humans (see pages 61-64). Verma et al. (Nature, 1997 Vol. 389:239-242) teach the problems of gene delivery in whole organisms using non-viral vector approaches, including liposomes as delivery agents, and state that such approaches suffer from limitations relating to poor efficiency of delivery and the transient expression of delivered genes (page 239, second paragraph from the end). Friedmann (Scientific American, 1997, pages 96-101) teaches that gene transfer by liposomes is much less efficient

than virus-mediated transfer (see pages 100 and 101, last and first paragraphs, respectively), while, according to Friedmann, the gene therapy field as a whole currently lacks convincing therapeutic benefit (see page 96). Branch (TIBS, February 1998 Vol. 23, pages 45-50) and Crooke (Stanley T. Crooke, 1998, Basic Principles of Anitsense Therapeutics, Springer-Verlag, NY, pages 1-50) teach that the *in vivo* (whole organism) application of nucleic acids (such as antisense) is a highly unpredictable endeavor due to target accessibility and delivery issues. Crooke also points out that cell culture examples are generally not predictive of *in vivo* inhibition of target cells (see entire text for Branch and pages 34-36 for Crooke).

While these references acknowledge the usefulness of gene therapy including lipid mediated delivery and the possibility of developing efficacious strategies in the future, they also illustrate that there are numerous obstacles to successful gene therapy which current methods still must overcome. As such, the disclosed utilities of the present specification which are drawn to gene delivery methods are credible. The present rejection, therefore is not for lack of utility, but rather for lack of enablement for the methods claimed.

(3) The amount of direction or guidance and the presence or absence of working examples. Applicants have not provided guidance in the specification toward a method of radiosensitizing *any* tumor tissue in *any* and all organisms comprising the administration of antisense using all methods of delivery which would avoid the technical obstacles recognized in the art as described above.

The specification teaches the radiosensitization of immunocompromised mice (e.g. Balb/C/nu/nu mice) subcutaneously implanted with SQ-20B tumor cells in which radiosensitization comprised the intratumoral administration of a phosphorothioated Raf

antisense oligonucleotide comprising the sequence 5'-GTGCTCCATTGATGC-3'. The specification fails to teach the successful delivery of antisense and subsequent inhibition of Raf in a whole organism. One skilled in the art would not accepts on its face the examples given in the specification of intratumoral administration of Raf antisense of known sequence in a mouse as being correlative or representative of the parenteral administration of antisense in any and/or all organisms such that the Raf gene or other genes are inhibited and further where treatment is provided in view of the lack of guidance in the specification and known unpredictability associated with the parenteral administration and *in vivo* delivery of antisense, including those encapsulated in liposomes, as cited in the references of Branch, Crooke, Schofield et al., Friedmann and Verma et al. as discussed above. The specification as filed fails to provide any particular guidance which resolves the known unpredictability in the art associated with *in vivo* delivery and treatment effects provided by antisense administered, and specifically regarding the instant Raf gene.

(4-5) The breadth of the claims and the quantity of experimentation required. The breadth of the claims is very broad. The claims are drawn to the radiosensitization of *any* cancer cell or tissue in *any* organism comprising the administration of antisense via *any* route to any organism. In order to practice the invention over the scope claimed, it would require trial and error or undue experimentation beyond which is taught in the specification to practice the invention drawn to any route of administration of an antisense to an organism such that Raf or any other gene is inhibited in a tumor tissue and further where treatment effects can be provided. The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of accessible target sites, modes of delivery and formulations to target appropriate

cell and/or tissues harboring Raf or other genes such that the genes are inhibited *in vivo* and further that treatment effects are provided. Since the specification fails to provide any particular guidance for the successful delivery of antisense in all organism for all tumors or cancers, and since determination of these factors for a particular antisense in a particular organism with a particular cancer is highly unpredictable, it would require undue experimentation to practice the invention over the scope claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Epand et al. [U.S. Patent No. 5,283,185].

Claim 1 is drawn to a composition comprising a cationic liposome containing a cationic lipid, phosphatidylcholine and cholesterol.

Epand et al. disclose the synthesis and use of cationic liposomes comprising a cationic lipid, phosphatidylcholine and cholesterol in an isotonic, pharmaceutically acceptable carrier (see Abstract, column 3, lines 7-21 and claim 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patel et al. (Molecular Carcinogenesis, 1993 Vol. 8:7-12), Kasid et al. (Science, 1989 Vol. 243:1354-1356), Monia et al. [U.S. Patent No. 5,952,229] in further view of Epand et al. [U.S. Patent No. 5,283,185] and Seung et al. (Cancer Research, 1995 Vol. 55:5561-5565).

The claimed invention is drawn to an (improved) method of treating a tumor comprising the administration of therapeutic radiation and further comprising the administration of antisense oligonucleotides, specific to an oncogene, encapsulated in liposomes, wherein the tumor is a laryngeal squamous carcinoma; wherein the cationic liposome is administered before the radiation, together, and separately.

Patel et al. teach the direct administration of antisense oligonucleotides to cancer cells (including those directed to Raf), in order to increase radiosensitivity of target cells (see Abstract and page 7).

Kasid et al. teach the effect of antisense c-raf-1 on tumorigenicity and radiation sensitivity of a human laryngeal squamous carcinoma. Kasid et al. further teach the introduction of antisense human c-raf-1 in radiation-resistant human laryngeal squamous carcinoma cells (SQ-20B) leads to a specific reduction in the steady-state levels of the endogenous c-raf-1 transcript, a reduced rate of SQ-20B tumor growth in nude mice, and to enhanced radiation sensitivity when compared with sense c-raf-1 transfectants or untransfected SQ-20B tumor cells (see Abstract and Figures 1-3).

Monia et al. teach the design, synthesis and use of antisense oligonucleotides of no more than 40 bases, comprising the sequence 5'-GTGCTCCATTGATGC-3' (see column 15, Table 8 and SEQ ID NO: 47), whereby the oligonucleotide is administered locally to the site of the tumor (see column 7, line 36 and column 8, line 4).

Patel et al., Kasid et al. and Monia et al. do not teach the encapsulation of antisense in cationic liposomes comprising phosphatidylcholine and cholesterol or systematic administration of the radiation and cationic lipid.

Epand et al. teach the synthesis and use of cationic liposomes comprising a cationic lipid, phosphatidylcholine and cholesterol in an isotonic, pharmaceutically acceptable carrier (see Abstract, column 3, lines 7-21 and claim 1).

Seung et al. teach combined gene therapy using cationic liposomes prior to radiation, together or separate with radiation overcomes tumor resistance to cytotoxic agents in murine tumor cells (see Abstract and Figures 2, 3 and 4).

It would have been obvious to one of ordinary skill in the art to design and administer antisense oligonucleotides directed to Raf to increase radiosensitivity of target tumor cells

because it was taught in the prior art that the expression of Raf oncogene was associated with the phenotype of radioresistance in cancer cells, and methods and compositions for reversing radiation resistance comprising the administration of antisense directed to Raf have been taught by Patel et al. and Kasid et al. One of ordinary skill in the art would have been motivated to construct an antisense oligonucleotide of no more than 40 bases since such antisense were explicitly taught by Monia et al. to inhibit expression of Raf. One of ordinary skill in the art would have a reasonable expectation of success since delivery of said antisense to tumor cells would lead to inhibition of Raf expression and would subsequently lead to increasing the radiosensitivity of target tumor cells, whereby administration of antisense targeted to the Raf gene had been taught in the prior art by Monia et al. using pharmaceutical compositions comprising antisense to Raf with liposomes as delivery agents for antisense. One of ordinary skill in the art would have been motivated to synthesize a cationic liposome composition for gene delivery comprising a cationic lipid, phosphatidlycholine, cholesterol and an oligonucleotide because these compositions have been taught in the prior art by Epand et al. as being capable of facilitating nucleic acid delivery into target cells, including cancer cells. One of ordinary skill in the art would have been motivated to use systematic administration of the cationic liposome prior to radiation, together or separate with radiation since Seung et al. taught that such combinations overcome tumor resistance to cytotoxic agents in murine tumor cells. One of ordinary skill in the art would have been reasonably successful in administering cationic liposomes prior to radiation, together or separate with radiation since the prior art explicitly taught such combinations (Seung et al.).

Therefore the invention as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (703) 306-3221. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 746-8693 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

tcg
October 18, 2002

SEAN McGARRY
PRIMARY EXAMINER
1635

Notice of References Cited	Application/Control No. 09/930,283	Applicant(s)/Patent Under Reexamination KASID ET AL.	
	Examiner Terra C. Gibbs	Art Unit 1635	Page 1 of 3

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-5,283,185	02-1994	Epand et al.	435/458
	B	US-5,952,229	09-1999	Monia et al.	435/375
	C	US-6,333,314	12-2001	Kasid et al.	514/44
	D	US-6,126,965	10-2000	Kasid et al.	424/450
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Crystal, R. Transfer of Genes to Humans: Early Lessons and Obstacles to Success. Science, 1995; Vol. 270:404-410.
	V	Schofield et a. Non-viral Approaches to Gene Therapy. British Medical Bullentin, 1995; Vol. 51:56-71.
	W	Verma et al. Gene Therapy-Promises, Problems and Prospects. Nature, 1997; Vol. 389:239-242.
	X	Friedmann, T. Overcoming the Obstacles. Scientific American, 1997; Vol. 276:96-101.

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

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	Examiner Terra C. Gibbs	Art Unit 1635	Page 2 of 3

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	A	US-			
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	N					
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	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Branch, A. A Good Antisense Molecule is Hard to Find. TIBS, 1998; Vol. 23:45-50.
	V	Crooke, ST. Basic Principles of Antisense Therapeutics, 1998 Springer-Verlag, NY, pages 1-50.
	W	Patel et al. Nucleotide Sequence Analysis of c-raf-1 cDNA and Promoter From a Radiation-Resistant Human Squamous Carcinoma Cell Line: Deletion Within Exon 17. Molecular Carcinogenesis, 1993 Vol. 8:7-12.
	X	Kasid et al. Effect of Antisense c-raf-1 on Tumorigenicity and Radiation Sensitivity of a Human Squamous Carcinoma. Science, 1989; Vol. 243:1354-1356.

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
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	Examiner Terra C. Gibbs	Art Unit 1635	Page 3 of 3

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FOREIGN PATENT DOCUMENTS

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	N					
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	Q					
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	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Seung et al. Genetic Radiotherapy Overcomes Tumor Resistance to Cytotoxic Agents. Cancer Research, 1995; Vol.55:5561-5565.
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Applicant: Usha KASID et al.

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Filing Date: August 16, 2001

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Examiner: Group Art Unit: 1635

U.S. PATENT DOCUMENTS

Examiner's Initials*		Document Number	Date MM/YYYY	Name (Family Name of First Inventor)	Class	Sub Class	Filing Date (if appropriate)
LK	AR	5,756,122	05/26/98	Thierry et al.			
LK	BR	5,283,185	02/01/94	Epand et al.	435	455	
LK	CR	5,952,229	09/14/99	Monia et al.	435	375	
	DR						
	ER						
	FR						
	GR						

FOREIGN PATENT DOCUMENTS

		Document Number	Date MM/YYYY	Country	Inventor Name		English Abstract		Translation Readily Available	
							Enclosed	No	Enclose	No
	HR									
	IR									
	JR									
	KR									
	LR									
	MR									
	NR									
	OR									
	PR									
	QR									

OTHER (Including in this order Author, Title, Periodical Name, Date, Pertinent Pages, etc.)

LK	RR	Crystal, r. 1995, Science Vol. 270, pages 404-410.
	SR	Verma, I. et al. 1997 Nature Vol. 389, pages 239-242.
	TR	Crook, S. 1998 Antisense Research and Application, Chapter 1, pages 1-50. Published by Springer-Verlag.
	UR	Friedmann, T. 1997 Scientific American. June, 1997, pages 96-101.
	VR	Lappalainen, K. et al. 1994 Pharmaceutical res. Vol. 11, No. 8, pages 1127-1131.
	WR	Schofield, J.P. et al. 1995 Brit. Med. Bull. Vol. 51, No. 1, pages 56-71.
	XR	James, W. 1991 Antiviral Chem and Chemotherapy Vol. 2, No. 4, pages 191-214.
	YR	Milner, N. et al. 1997 Nature Biotech. Bol. 15, pages 537-541.
LK	ZR	Patel, CK. Et al. 1993. Molecular Carcinogenesis, Vol. 8, pages 7-12.

Examiner [signature] Date Considered: 10/15/02

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